

Remarks

Claims

Claim 15 has been amended to recite "... a plurality of a at least ..." This amendment adds no new matter. Entry and consideration of claims 15-17 is respectfully requested.

Claim Objection

Applicants have amended claim 15 to recite "... a plurality of a at least ..." as the Examiner has requested. Reconsideration and removal of the claim objection is requested.

Claim rejections under 35 U.S.C. §103

Claims 15-17 were rejected under 35 U.S.C. §103(a) as being unpatentable over King et al. (US2004/0014202) in view of Pinkel et al. (US 5,837,196) and Glazer et al. (US 6,150,107).

Before commenting on the prior art, Applicants would like to explain once more the principle of operation of the invention. The invention aims at a real time PCR instrument for detecting maximum fluorescence emission of at least five different fluorescent compounds. Referring to Figure 4 as an example of possible embodiment for the instrument of the invention, the instrument has an excitation unit comprising a light source (LED) that emits light toward a reaction vessel. A lightpipe is arranged for receiving the light from the reaction vessel and is capable of distributing this light homogeneously to a fiber bundle. The fiber bundle (at least 5) transmits this light to at least 5 separate fluorescent detector entities in the detection unit, each of said detector entities having central detection wavelengths distinct from each other by at least 25 nm. The instrument has also means for heating and cooling and multiple reaction vessels to conduct the necessary heating and cooling steps of the PCR reaction. The excitation and the detection units are located in separate housings.

There are many advantages provided by the specific arrangement of the instrument according to the invention. One of these advantages is that only one light source, e.g. a monochromatic light source such as for example a LED emitting at 470 nm, is potentially necessary for detecting the fluorescence of at least 5 different fluorescent compounds simultaneously in multicolor real time PCR reactions. The instrument requires neither multiple excitation light sources (with different wavelengths) nor filters for exciting different fluorescent

compounds. Because the excitation and detection units are decoupled and separated by using optical fibers and because a lightpipe homogeneously distributes the light to these fibers, highly precise positioning of the excitation unit towards the reaction vessel can be achieved without moving the detection unit. Also, the number of necessary dichroic mirrors is minimized by this arrangement.

This is clearly stated on page 17, lines 19-27 of the patent application as filed:

"This set up of excitation unit and detection unit located in separate housings provides two advantages compared to the optical unit as disclosed in WO 97/46712: Homogeneous distribution of emitted light into all six detection channels and mechanical decoupling of the excitation and detection unit. This enables highly precise positioning of the excitation unit towards the reaction vessels to become monitored (e. g. capillary tips) without moving the detection unit. Moreover, the number of necessary dichroic mirrors is minimized. An example of such a set up is shown in fig. 4, which discloses a possible embodiment of the invention. As it can be seen, excitation and detection unit are located in different housings."

Applicants believe that these features are fully reflected in amended claim 15 and that the Examiner fails to completely appreciate all the features of claim 15.

In particular, the Examiner alleges that King et al. discloses a real time PCR instrument. The Examiner has stated that the Applicant has not defined "device" and "instrument" in the specification as filed. This distinction is not relevant. Applicants respectfully assert that King et al does not teach either a "device" or an "instrument" which carries out thermalcycling in a manner which conducts PCR. Thus, King et al. do not teach a PCR instrument at all, as taught by the instant invention..

The Examiner again alleges that King et al. teach a device having a detection unit comprising at least 5 separate fluorescent detector entities, each of said detector entities having a central detection wavelength distinct from each other by at least 25 nm. The Examiner points to page 3, paragraph [0028] of King. However, we reiterate that King et al. only discloses different dyes, having different emission wavelengths and detectors, some of them could be separated by more than 25 nm in their wavelengths. Further, in paragraph [0078], King et al. describes that

when multiple OLED are used, they are capable of producing excitation wavelengths at four different frequencies, implying the identification of only four distinct fluorescent compounds, not five. King et al. does not teach specifically that the central detection wavelength of these detector entities must be distinct from each other by at least 25 nm.

The Examiner alleges that King et al. teaches a lightpipe being arranged for receiving light from the reaction vessel and capable of distributing homogeneously said light for transmission to optical fiber bundles. The Examiner relies on paragraph [0043] of King et al. Applicants respectfully disagree. A careful reading of paragraph [0043] of King et al. teaches that the device for carrying wavelengths is either a lightpipe or fiber optics, mirror, and/or lenses, not a combination of a lightpipe and optical fibers. Further, King et al. fails to disclose 5 optical fiber bundles. Also, and in any cases, King et al. fails to teach the specific location of the optical fibers toward the lightpipe and their interaction with the lightpipe, i.e. King et al. fails to teach that the lightpipe receives light from the reaction vessel and that the light is then distributed to the optical fiber bundles (and not the other way around for example).

The Examiner also alleges that in Fig. 7, King et al. teaches a device wherein the excitation and detection units are located in separate housings. The Examiner merely points to Figure 7 in King where the detector and excitation units are represented by different schematic symbols. The excitation unit of the device of the invention comprises at least one light source and a lightpipe and the detection unit comprises detector entities. Thus, in the device of the invention, the excitation unit (light source + a light pipe) are located in one housing and the detectors are located in a separate housing. Again, Fig. 7 in King et al. does not teach this specific arrangement. Fig. 7 in King et al. teaches a light source, two lightpipes and two detectors. In Fig. 7, the excitation unit (light source + lightpipe) are not located in a single housing that is separate from the detectors. Furthermore, the detectors are not located in a housing.

The Examiner has admitted that King fails to teach at least 5 optical fiber bundles. However, the Examiner has incorrectly relied on Pinkel stating that Pinkel teaches at least 5 optical fiber bundles by pointing to the Abstract of Pinkel. Nowhere in the Abstract of Pinkel are at least 5 optical fiber bundles taught. The Examiner has merely vaguely stated that Pinkel et al., “[b]y teaching a plurality of groups of optical fibers ... teach a plurality of at least 5 optical fiber

bundles.” However, nowhere in the abstract that the Examiner has pointed to are “at least 5 optical fiber bundles” taught, and the Examiner has failed to show this.

Pinkel et al. teach a bundle of optical fibers dipped in the reaction medium and transmitting directly the light emitted from the reaction vessel to multiple detectors. Apart from teaching the use of optical fibers in a detection method, Pinkel et al. does not provide any teaching that could be useful to arrive at the invention. In particular, the device taught in Pinkel et al. is completely inadequate for the intended purpose of the instrument according to the invention, which is detecting the fluorescence of at least 5 different fluorescent compounds simultaneously in multicolor real time PCR reactions. There is no element allowing a real time PCR reaction in the device taught by Pinkel et al. Further, Pinkel et al. does not teach the benefits of the instrument according to the invention regarding the separation of the excitation and detection units in separate housings either, the precision obtained and the minimization of dichroic mirrors. Therefore, the person skilled in the art would not even have been motivated to take into account the teaching of Pinkel et al. to arrive at the invention.

Glazer et al. does not provide any additional teaching in this regard either.

Even by combining King et al. with Pinkel and Glazer, some of the most critical elements of the instrument of the invention as recited above are still missing. In particular, all of King et al. with Pinkel and Glazer fail to teach an excitation unit and a detection unit that are located in separate housings and the benefits associated thereto as explained above. Even by combining the teaching of all three references, the person skilled in the art would still miss this critical teaching and would therefore also miss the motivation to implement this critical feature in a PCR instrument.

Applicants therefore respectfully submit that the instrument as presently claimed in claim 15 is not obvious over the prior art of records. Reconsideration and withdrawal of the obviousness rejection of claim 15 under §103(a) as being unpatentable over King et al. (US2004/0014202) in view of Pinkel et al. (US 5,837,196) and Glazer et al. (US 6,150,107) is respectfully requested.

Claims 16 and 17 depend upon claim 15 and therefore incorporate each and every limitation of that claim. For the reasons set forth with respect to claim 15, withdrawal of the rejections of the dependent claims 16 and 17 is also respectfully requested.

Conclusion

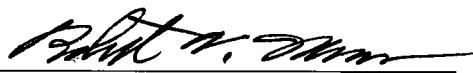
The shortened statutory period of three months originally set for responding to the Office Action expired on November 21, 2009. A three-month extension of time is therefore requested. The extension of time resets the deadline for responding to February 21, 2010. The Commissioner is authorized to charge the corresponding fee under 37 CFR 1.17(a)(2) to Account No. 50-0812. No other fee is believed to be due at this time, however, the Commissioner is authorized to charge any fee deficiency, or credit any overpayment, to Deposit account No. 50-0812.

Applicants believe that the present application is now in condition for allowance. No other fee is believed to be due at this time. The Commissioner is further authorized to charge any fee deficiency or credit any overpayment to the Deposit Account No. 500812.

If the Examiner believes that a telephone call would expedite prosecution of this application, the Examiner is invited to call the undersigned directly at the number below.

Respectfully submitted,

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Robert W. Mann (Reg. No. 48,555)

Roche Molecular Systems, Inc.
4300 Hacienda Drive
Pleasanton, CA 94588
Tel. 925-730-8560
Fax 925-225-1128